Remarks

The Office Action asserts that newly submitted claim 43 is directed to an invention that is independent or distinct from the invention originally claimed because the new claim is of a different species than previously claimed. The Office Action asserts that a different lubricant is being claimed that was not previously claimed. Claim 43 has been withdrawn.

Claims 41 and 42 were previously withdrawn.

Rejections

35 U.S.C. §103(a)

Claims 1, 3, 5 and 6 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. U.S. Patent No. 5,667,840 ('840) in view of U.S. Patent No. 5,082,630 to Partin et al.

The Office Action asserts that:

> Tingey discloses a method for detecting the presence and uniformity of a lubricious coating on a medical device comprising the steps of preparing a mixture of at least one fluorescing agent and at least one lubricant; applying said mixture to the surface of a medical device, subjecting the surface of the medical device to a source of energy capable of inducing a fluorescing emission; and observing the fluorescent emission (column 2, line 64 – column 3, line 7). Tingey discloses the claimed invention except for the specific fluorescing agent being a fluorescein or a rhodamine. Partin teaches that fluorescein and rhodamnine are fluorescent dyes that have good absorption and fluorescent yield characteristics that provide high sensitivity. It would have been obvious to one having ordinary skill in the art at the time the invention was made to provide the device, of Tingey with a rhodamine or a fluorescein fluorescent agent since these agents have good absorption and fluorescent yield characteristics.

Applicants traverse the rejection.

Claim 1 of the present application is directed to a method for detecting the presence and uniformity of a lubricious coating on a medical device comprising the steps of preparing a mixture of at least one fluorescing agent which is a *xanthene, a triarylmethane or mixture thereof* and at least one lubricant; applying said mixture to the surface of a medical device to form a coating capable of exhibiting fluorescence; subjecting the surface of the medical device to a source of energy capable of inducing a fluorescent emission; and observing the fluorescent emission to determine the location, uniformity or both of said lubricant.

As discussed in the previous response mailed December 22, 2003, Tingey et al. disclose only coumarin fluorescent dyes for use in combination with a polydimethylsiloxane lubricant disclosed therein. Furthermore, Tingey et al. teach that in order to be effective, the fluorescent agent **must** have a degree of solubility in polydimethylsiloxane:

> *In order to be effective in this application, the fluorescent agent must have a degree of solubility in polydimethylsiloxane. Polydimethylsiloxane is an extremely hydrophobic material,* ***and most fluorescent dyes are virtually insoluble*** *it [sic].* As is reported above and in the cited references as an example, an individual medical device, such as the intravenous catheter, has only about 0.3 mg of polydimethylsiloxane of 12,500 cs lubricant applied to it. Thus, given the size and surface area of the part, the coating of polydimethylsiloxane on the device surface is less than about 1×10^{-3} mm thick. This fact, coupled with the physical properties of the polydimethylsiloxane, renders addition of even an intensely colored dye to the polydimethylsiloxane for visualization of the coating of little utility. Additionally, since a catheter is a medical device, addition of a substantial amount of a strongly colored dye is undesirable and subjects the device to additional approval steps. *Further, most common dyes are only dispersible, not soluble, in polydimethylsiloxane. A trial where about 0.3 percent (wt./wt.) of an intensely colored violet dye, Calco oil violet ZIRS, available from BASF Corp.,* ***was only dispersed, not dissolved, in polydimethylsiloxane, did not allow an observer to easily determine if a uniform coating of polydimethylsiloxane was present on the catheter.***
>
> Col. 4, lines 32-55, emphasis added

Consequently, Tingey et al. suggest that most fluorescent dyes are virtually insoluble in polydimethylsiloxane, and if they are only dispersed, not dissolved in the polydimethylsiloxane, the observer could not easily determine if a uniform coating of polydimethylsiloxane was present on the catheter. Thus, from the above paragraph, it can be concluded that most fluorescent dyes cannot be employed in the method of Tingey et al.

The Office Action asserts on page 5, paragraph no. 9, that Tingey et al. '840 also disclose that other dyes than those listed may be used (column 4, line 56 – column 5, line 16). However, Tingey et al.'s list includes *only specific coumarin dyes*, not other classes of dyes. Consequently, while such a statement might suggest that some other specific coumarin dyes not listed therein may be used, there is no basis to interpret the statement as suggesting that other *classes* of dyes may be used.

Furthermore, Tingey et al. at column 4, lines 64-66, make the following statements: "The preferred dyes are soluble in 12,500 cs. polydimethylsiloxane. The preferred dyes fluoresce strongly about 510 nm (yellow-green) when excited with the preferred UV radiation."

Consequently, Applicants submit that there is no suggestion by Tingey et al. to employ other than coumarin dyes, or dyes that have a specific ***known*** solubility in polydimethylsiloxane of 12,500 cs.

The Office Action asserts, middle of page 3, that "Partin teaches that fluorescein and rhodamine are fluorescent dyes that have good absorption and fluorescent yield characteristics that provide high sensitivity. It would be obvious to one having ordinary skill in the art at the time the invention was made to provide the device, of Tingey with a rhodamine or a fluorescein fluorescent agent since these agents have good absorption and fluorescent yield characteristics."

Applicants disagree.

Partin et al. disclose a portable fiber optic detector that senses the presence of specific target chemicals in air or a gas by exchanging the target chemical for a fluoroescently-tagged antigen that is bound to an antibody which is in turn attached to an optical fiber. Replacing the fluorescently-tagged antigen reduces the fluorescence so that a photon sensing detector records the reduced light level and activates an appropriate alarm or indicator (Abstract).

Partin et al. are silent as to lubricants and to polydimethylsiloxane solubtiliy.

As Partin et al. do not suggest fluorescent dyes in combination with lubricants, and there is no suggestion by Tingey et al. to employ other than coumarin dyes, or dyes that have a specific known solubility in polydimethylsiloxane of 12,500 cs, this combination of references fails to suggest the specific dyes of claim 1 according to the present invention in a lubricant for medical devices.

Furthermore, Applicants submit that there would be no motivation to combine these references.

> When a rejection depends on a combination of prior art references, there must be some teaching, suggestion, or motivation to combine the references. *In re Geiger*, 815 F.2d 686, 688 [2 USPQ2d 1276] (Fed. Cir. 1987). Although the suggestion to combine references may flow from the nature of the problem, *Pro-Mold & Tool*

> *Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 [37 USPQ2d 1626] (Fed. Cir. 1996), the suggestion more often comes from the teachings of the pertinent references, *In re Sernaker*, 702 F.2d 989, 994 [217 USPQ 1] (Fed. Cir. 1983), or from the ordinary knowledge of those skilled in the art that certain references are of special importance in a particular field, *Pro-Mold*, 75 F.3d at 1573 (citing *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 297 n.24 [227 USPQ 657] (Fed. Cir. 1985)). Therefore, "[w]hen determining the patentability of a claimed invention which combines two known elements, 'the question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination." *In re Beattie*, 974 F.2d 1309, 1311-12 [24 USPQ2d 1040] (Fed. Cir. 1992) (quoting *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452, 1462 [221 USPQ 481] (Fed. Cir. 1984)).

Akamai Technologies Inc. v. Cable & Wireless Internet Services Inc., 68 USPQ2d 1186. 1193 (CA FC 2003).

Applicants submit that because Tingey et al. suggest only specific coumarin dyes, or dyes with a solubility in polydimethylsiloxane of 12,500 cs, and further suggest most dyes are insoluble and thus ineffective for use therein, there is no suggestion or motivation to combine the fluorescent dyes of Partin et al. with the method of Tingey et al. because there is nothing to suggest the desirability, and therefore the obviousness of making this combination.

Furthermore, hindsight was improperly employed in finding claim 1 of the present application unpatentable. A proper obviousness analysis is one which is used to assess the invention as whole to determine whether there was suggestion or motivation to combine the prior art references without engaging in improper hindsight determination. Motivation to combine the references may be found in nature of problem to be solved. See *Ruiz v. A.B. Chance Co.*, 69 USPQ2d 1686 (CA FC 2004).

Applicants submit that there would be no motivation to combine these references because the problems to be solved are quite different. Partin et al. describe attachment of antibodies to the distal end of an optical fiber or waveguide and saturating the antibodies with a fluorescently-tagged antigen. When exposed to an air sample, a decrease in fluorescence indicates the presence of the suspect chemical compound in the air sample. Attachment of the fluorescent tags to the antigen molecules requires a reactive site on the antigen molecule and must not interfere with the binding of the antigen to the drug antibody. See Summary of the

Invention.

Tingey et al., desires fluorescent dyes which, in order to be effective, are soluble in, and can be mixed with polydimethylsiloxane.

There is no basis for predicting that a fluorescent dye which can be attached to an antigen, would have the solubility necessary to be effective as a fluorescing agent when mixed with polydimethylsiloxane lubricant. The two properties are not related in any known way.

The use of improper hindsight in the Examiner's analysis is evident in the following statements, made on page 5 of the Office Action, are evidence of this:

> Applicant discloses that it is difficult to dissolve the dye directly in polydimethylsiloxane (paragraph 55). Applicant admits that the chosen dyes have a degree of solubility in polydimethylsiloxane since it is said to be difficult, but not impossible to dissolve the preferred dyes in polydimethylsiloxane. Tingey et al. '840 also discloses that other dyes than those listed may be used (column 4 line 45 – column 5 line 16). Since applicant has admitted that the preferred dyes have a degree of solubility in polydimethylsiloxane, the method of Tingey could be used with dyes as claimed by Applicant.

Applicants submit that Applicants' statements should not be part of the analysis. Applicants' application is not part of the prior art. The obviousness analysis should be based on the teachings of the prior art alone.

Applicants further submit that the statement that some dyes may be suspended, and not fully solubilized in the polydimethylsiloxane (see paragraph 55, second sentence), is not an admission of any sort. Applicants have not indicated that dyes which are suspended rather than solubilized cannot be used, but only have indicated that it may be desirable in such situations to employ a solvent or cosolvent blend. Applicants submit that this is not an admission of solubility, and certainly not an admission of ***known*** solubility.

Tingey et al. make the statement that "[i]n order to be effective in this application, the fluorescent agent ***must*** have a degree of solubility in polydimethylsiloxane." (emphasis added) Tingey et al. indicate that this degree of solubility as being 12,500 cs in polydimethylsiloxane. See col. 4, lines 32-35 and lines 63-65.

The examiner then draws the conclusion that "[s]ince applicant has admitted that the preferred dyes have a degree of solubility in polydimethylsiloxane, the method of Tingey

could be used with dyes as claimed by Applicant." Applicants submit that this too is an improper analysis. The analysis should not be whether the preferred dyes of the present application can be used in the method of Tingey et al. The correct analysis is whether or not there is a suggestion and motivation to employ the dyes of Partin et al., with the method of Tingey et al. to render claim 1 obvious. Applicants' statements or teachings cannot be used in the obviousness analysis. That is improper hindsight.

Applicants submit that for all of these reasons, claim 1 of the present application is not obvious over Tingey et al. in view of Partin et al. Claims 3, 5 and 6 depend from claim 1 and are patentable for at least the reasons that claim 1 is patentable.

Applicants respectfully request withdrawal of the rejection of claims 1, 3, 5 and 6 under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of U.S. Patent No. 5,082,630 to Partin et al. Claims 4, 39 and 40 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 5,346,689 to Peyman et al.

The Office Action asserts that Tingey et al. discloses the claimed invention except for the specific fluorescing agent being a carboxyfluorescein.

Applicants traverse the rejection.

Claims 4 and 39 depend from claim 1.

Claim 1 has been discussed above.

Tingey et al. and Partin et al. have been discussed above.

Peyman et al. disclose a method of performing angiography by using calcein as the fluorescent indicator substance and also to a method of performing photocoagulation therapy and angiography. (see Background of the Invention, col. 1, lines 10-13).

Also, in the Background of the Invention, Peyman et al. discuss the use of carboxyfluorescein:

> Carboxyfluroescein is another fluorescent dye which has been used for fundus angiography. Carboxyfluorescein is a hydrophilic derivative of fluorescein. The light absorption peak of carboxyfluorescein is 490 nm and it fluoresces maximally at 520 nm. Carboxyfluorescein has a molecular weight of 373. The main distinction between carboxyfluorescein and sodium fluorescein is that carboxyfluorescein has 1/1000 the lipid solubility of sodium fluorescein and thus is less likely to penetrate cell membranes. Studies of carboxyfluroescein used in

> fluorophotometry to investigate blood-ocular barriers indicate that it may delineate certain abnormalities of these barriers better than sodium fluorescein. Because carboxyfluorescein is not as readily glucuronated as sodium fluorescein, carboxyfluorescein also has been used as a tracer in quantitative physiological studies of the anterior chamber of human eyes.
>
> Col. 1, lines 43-59

Peyman et al. is silent as to using carboxyfluorescein with lubricants. As Tingey et al. suggest only coumarin fluorescent dyes, or those dyes having a solubility of 12,500 cs in polydimethylsiloxane, as discussed above, and Tingey et al. also suggest that most dyes are dispersible only in polydimethylsiloxane, and therefore not effective (see col. 4, lines 32-35, lines 50-55, and lines 63-65) there is no motivation to combine the hydrophilic carboxyfluorescein dye described by Peyman et al. with the polydimethylsiloxane lubricant of Tingey et al. One clearly is lead by this art to expect that Peyman et al.'s dyes are insoluble dyes and therefore ineffective in the method of Tingey et al.

Independent claim 40, which is directed to the use of a hydrophilic dye in combination with a hydrophobic lubricant is patentable for at least the same reasons that independent claim 1 is patentable. Tingey et al. suggest only coumarin fluorescent dyes, or those having a degree of solubility in polydimethylsiloxane of 12,500 cs. This does not lead one to select a hydrophilic dye.

Applicants submit that there is no suggestion or motivation to combine the references Partin et al. and Peyman et al. with Tingey et al., and therefore, claim 40 is also patentably distinguishable over the combination of references.

Applicants respectfully request withdrawal of the rejection of claims 4, 39 and 40 under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 5,346,689 to Peyman et al. Claim 7 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 6,254,634 to Anderson et al. The Office Action asserts that:

> Tingey, as modified, discloses the claimed invention except for the use of a lubricant in combination with a crosslinkable silicone. Anderson teaches that an intermediate layer of crosslinkable silicone is provided with a coating in order to improve the performance and durability of the coating by preventing the lubricant

from being wiped off the surface of the coated evice [*sic*] (Column 2 lines 54-59, Column 3 lines 41-52 and Column 5 lines 42-64). It would have been obvious to one having ordinary skill in the art at the time the invention was made to provide the method of Tingey, as modified, with the crosslinkable silicone in order to improve the durability of the coating on the medical device.

Applicants traverse the rejection.

Claim 7 depends from claim 1.

Claim 1 has been discussed above.

Tingey et al. and Partin et al. have been discussed above.

Anderson et al. disclose an article (e.g., in the form of an implantable medical article) comprising a support material bearing an intermediate layer comprising a functional silicone polymer formulation, the intermediate layer having photoimmobilized thereon a target compound. In a preferred embodiment, the functional silicone polymer formulation comprises a hydride functional siloxane polymer formulation (Summary of the Invention, 1st paragraph).

Anderson et al. disclose fluorescent agents generally. See column 9, lines 60-65.

Applicants assert that combining the silicone polymer formulation comprising hydride functional siloxane polymer formulation with Tingey et al. would, at most, with lead one of skill in the art to employ the coumarin fluorescent dyes of Tingey et al., or those dyes having a known solubility of 12,500 cs in polydimethylsiloxane. As discussed above, there is no suggestion or motivation to employ the fluorescent dyes of Partin et al. with the lubricants of Tingey et al. because Part et al.'s dyes are not coumarin dyes and are not shown to have a known solubility in polydimethylsiloxane. Consequently, there is no motivation to employ these fluorescent dyes of Partin et al. with the silicone polymer formulation of Anderson et al., as the same reasons apply.

Applicants respectfully request withdrawal of the rejection of claim 7 under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 6,254,634 to Anderson et al. Claims 8-11 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 5,266,359 to Spielvogel. The Office Action asserts that:

Tingey, as modified, discloses the claimed invention except for the mixture

further comprising a surfactant. Spielvogel teaches that a surfactant may be added to a medical device in order to improve the lubriciousness of the device (Column 2 lines 49-56 and Column 4 lines 38-52). It would have been obvious to one having ordinary skill in the art at the time the invention was made to provide the device of Tingey with the surfactant of Spielvogel in order to improve the lubricity of the device.

Applicants traverse the rejection.

Claims 8-11 depend from claim 1.

Claim 1 has been discussed above.

Tingey et al. and Partin et al. have been discussed above. Claim 1 is patentable over this combination for the reasons presented above.

Spielvogel discloses a lubricating composition including an emulsion of a noncuring polysiloxane, a surfactant and water (Abstract). Spielvogel is silent as to fluorescing agents. Combining Spielvogel with Tingey et al., would, at most, lead one of skill in the art to the coumarin fluorescent agents of Tingey et al., or those fluorescent agents having a degree of solubility in polydimethylsiloxane of 12,500 cs. There is no motivation to combine Partin et al. with Tingey et al. for the reasons discussed above. Consequently, this combination fails to render claim 1 obvious for the same reasons as previously given.

Claims 8-11 depend from claim 1 and are patentable for at least the reasons that claim 1 is patentable. Applicants respectfully request withdrawal of the rejection of claims 8-11 under 35 U.S.C. §103(a) as being unpatentable over Tingey et al. '840 in view of Partin et al., as applied above, and further in view of U.S. Patent No. 5,346,689 to Peyman et al.

CONCLUSION

Claims 1, 3-11, 39 and 40 are pending in the application. Applicants have addressed each of the issues presented in the Office Action. Based on the foregoing, Applicants respectfully request reconsideration and an early allowance of the claims as presented. Should any issues remain, the attorney of record may be reached at (952)563-3011, to expedite prosecution of this application.

Respectfully submitted,

VIDAS, ARRETT & STEINKRAUS

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By: _____
Lisa R. Lindquist
Registration No.: 43071

6109 Blue Circle Drive, Suite 2000
Minnetonka, MN 55343-9185
Telephone: (952) 563-3000
Facsimile: (952) 563-3001

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